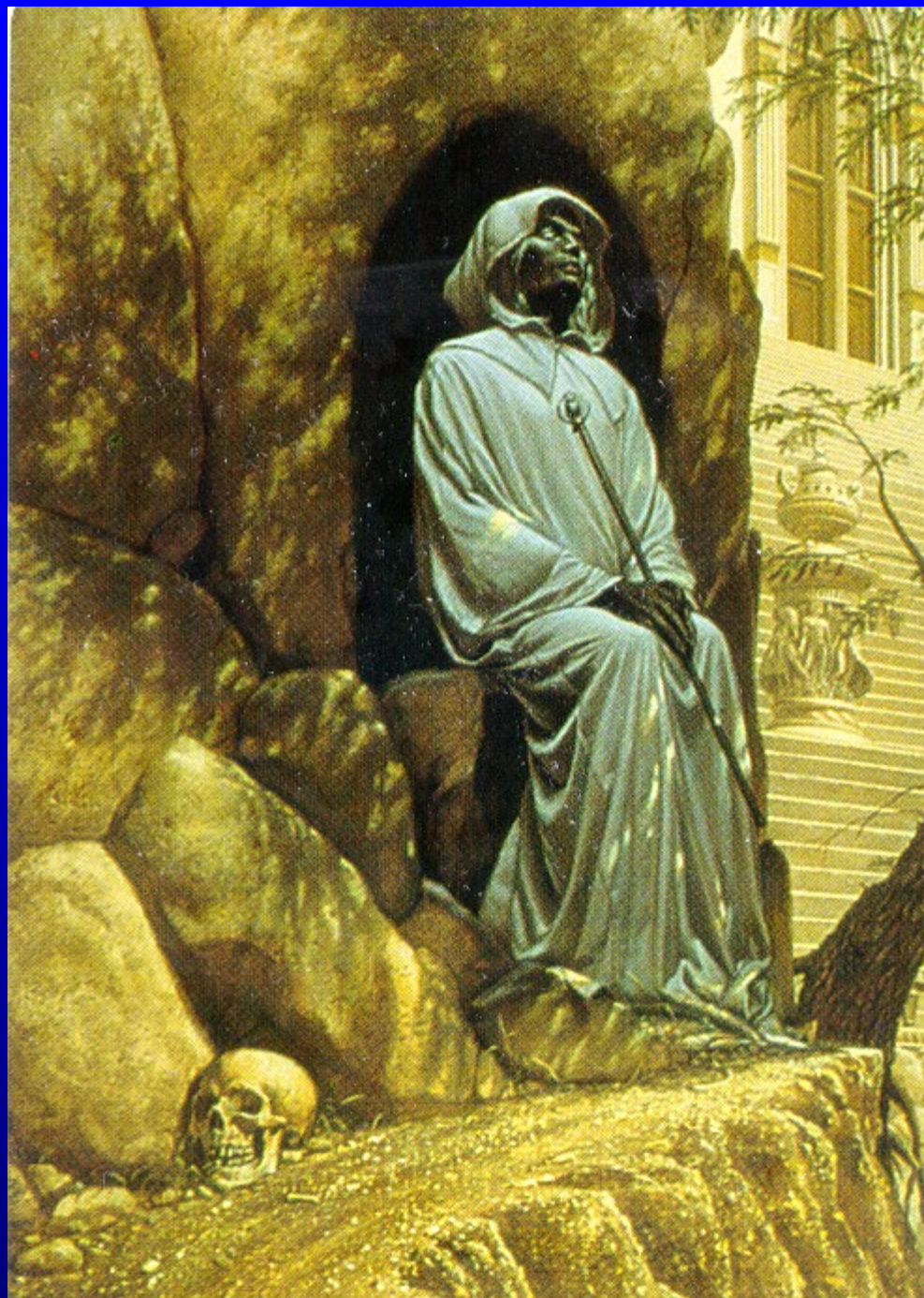


Lymphadenopathy -- Approach to evaluation/work up for the Internist

Jeremy G. Perkins, MD
PGY-2 Internal Medicine
Walter Reed Army Medical
Center

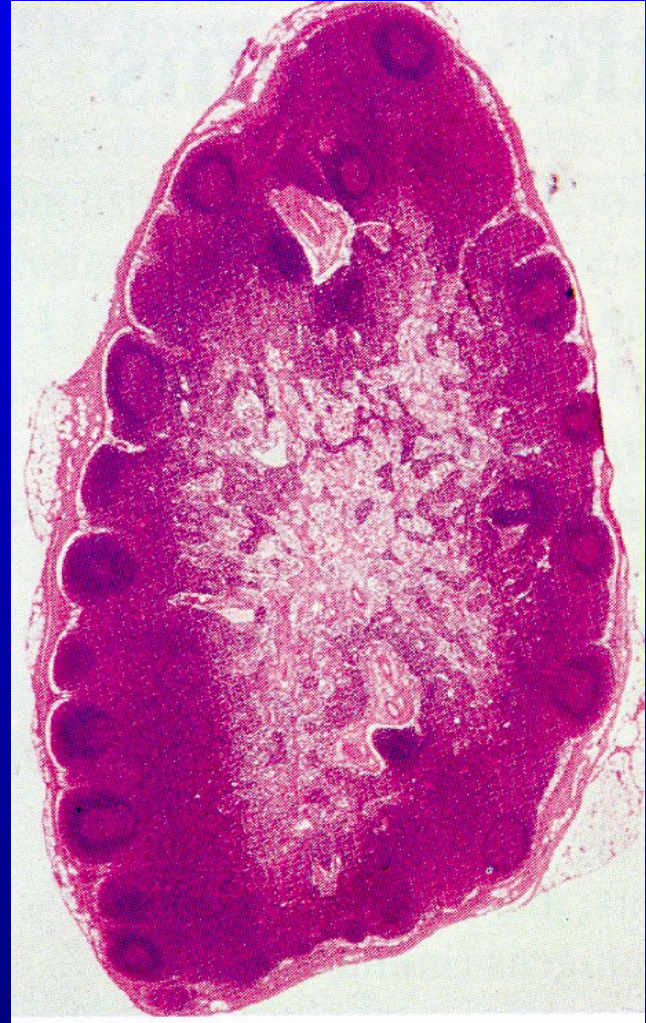


Lecture Outline

- Definition
- Epidemiology
- Risk Factors
- History
- Environmental/Occupational Exposures
- Physical Exam
 - Localization
 - Associated Findings Specific to Conditions
- Diagnostic Approach
- Excisional Biopsy
- Summary

Definition

- Approx 600 LN in body
- LAN = abnl size, number, consistency
- Generalized vs Local
- Peripheral (central LAN presents differently)



Epidemiology

In the primary care setting, 0.6% annual incidence

Of 2556 cases, 256 (10%) referred onward

Of the 256, only 82 (3.2 of total) went to Bx

Of the 82 Bx, only 29 (1.1% of all cases)

Risk Factors to Keep in Mind

- Size Matters!!

- In one series of 213 adults with unexplained LAN who went on to biopsy
 - LN <1 cm - 0% malignancy
 - LN 1-1.5 cm - 8% malignancy
 - LN > 1.5x1.5 (2.25 cm²) - 38% malignancy

- Age Matters!!

- Age > 40, malignancy is more common
- (Age >40 = 4% vs Age < 40 = 0.4%)

- Location Matters!!

- Supraclavicular has the highest risk of Malignancy - est at 90% in patients >40 and 25% in ages < 40

History

- URI sx's? Conjunctivitis sx's?
- Infections/Bites/Cuts/Abrasions/Dermatitis?
- Recent Immunizations?
- Immunocompetence (HIV etc)
- Constitutional Symptoms?
 - F/C/NS, Wt loss, fatigue/malaise
 - Suggests infx, collagen-vasc dz, or malignancy
- Has there been an environmental (travel, pets) or occupational exposure to explain disease?
- Sexual history? -- if inguinal LAN

Environmental Exposures

General -

Cat Exposure - Cat-scratch dz, Toxo

Under-cooked meat - Toxo

Tick-Bite - Lyme's Dz, Tularemia

TB Symptoms - TB Adenitis/Scrofula

Recent Blood transfusion - CMV

High-Risk Sexual Behavior - HIV, syphilis,
HSV, CMV,

Hep B

IVDU - HIV, endocarditis, Hep B, Hep C

Occupational Exposure



Infantry?

Huah!

Occupational Exposures



Armor?

Mechanics?

Occupational Exposures

- Hunters/Trappers -
Tularemia/Lyme Dz
- Fishermen/Slaughterhouse
Workers - *Erysipelothrix*
rhusiopathiae (Erysipeloid)

Travel History



Masai Child



“Where you stand depends
on where you sit”

Travel Exposures

- East Africa/Mediterranean, China, Latin America
 - Kala-Azar (visceral leishmaniasis)
- Mexico, Peru, Chile, India, Pakistan, Egypt, Indonesia
 - Typhoid Fever (salmonella)
- Southeast Asia, India, Northern Australia
 - Scrub Typhus
- Arizona, SW California, New Mexico, Western Texas
 - Coccidiomycosis
- Southeastern/Central US “Mississippi River Valley”
 - Histoplasmosis
- Southwestern US
 - Bubonic Plague

Medications which can cause LAN

- Phenytoin, Tegretol
- Atenolol, Captopril, Hydralazine
- PCN, Cephalosporins, Sulfonamides
 - assoc with “serum-sickness” allergic reaction marked by fevers, rash, and arthralgias
- Allopurinol
 - usually assoc with skin eruptions (exfoliative dermatitis, TEN) or systemic febrile illness
- Gold, quinidine, pyrimethamine, sulindac, primidone

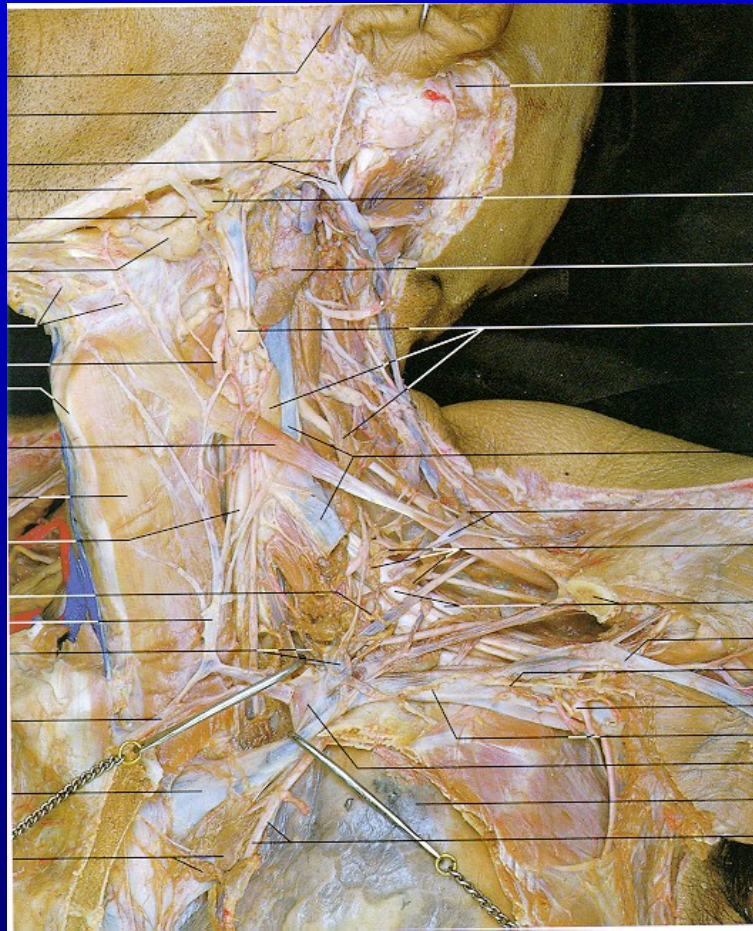
Physical Examination

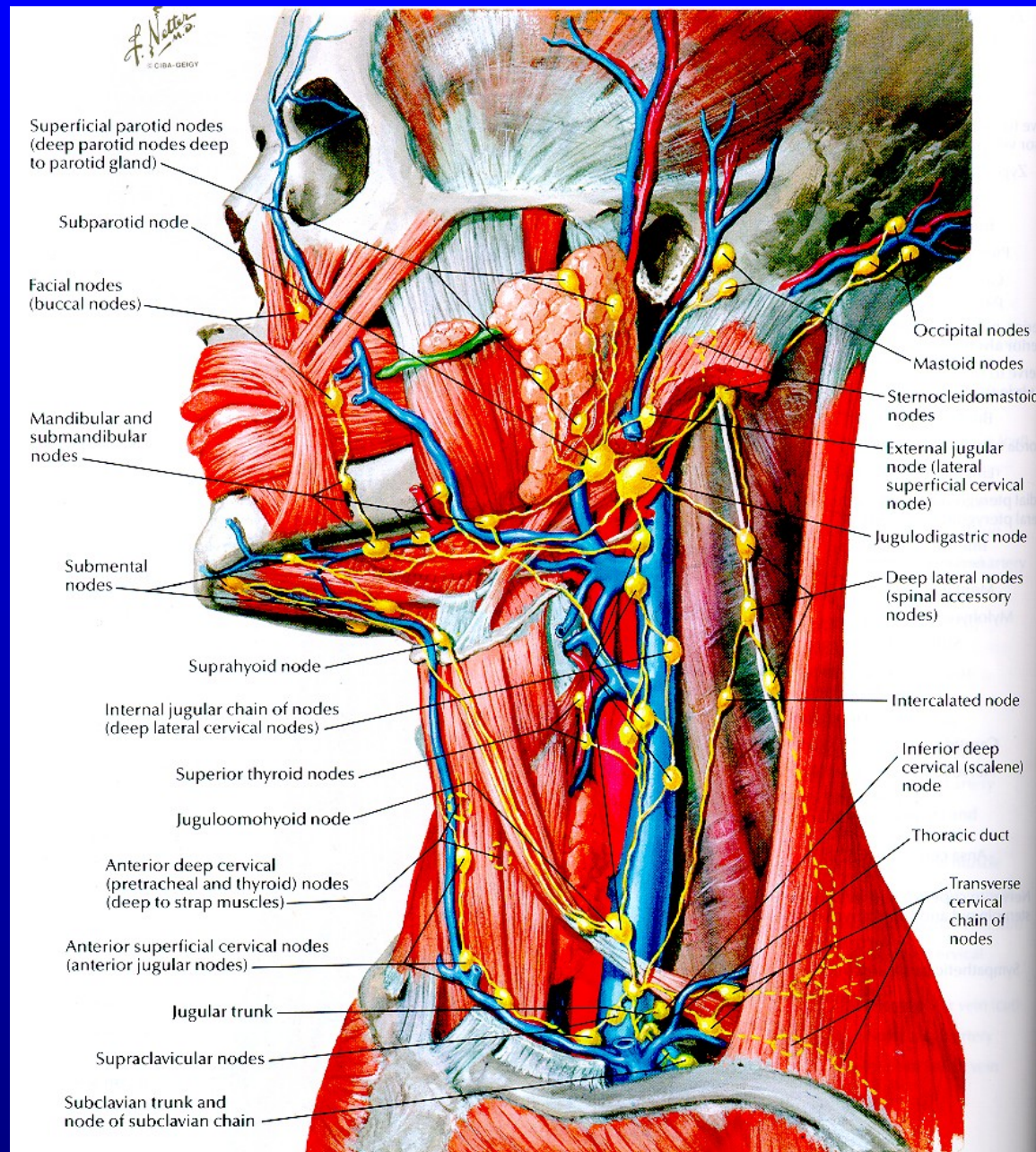
- Size (cm)
- Consistency
 - Stony/Hard - concerning for cancer
 - Soft Nodes - infection/inflammatory condition
 - Firm/Rubbery Nodes - suggestive of lymphoma
- Pain/Tenderness - the result of rapid increase in size - usually the result of inflammatory process though could be hemorrhage into a necrotic malignant node

Location of involvement can help suggest etiology

Cervical

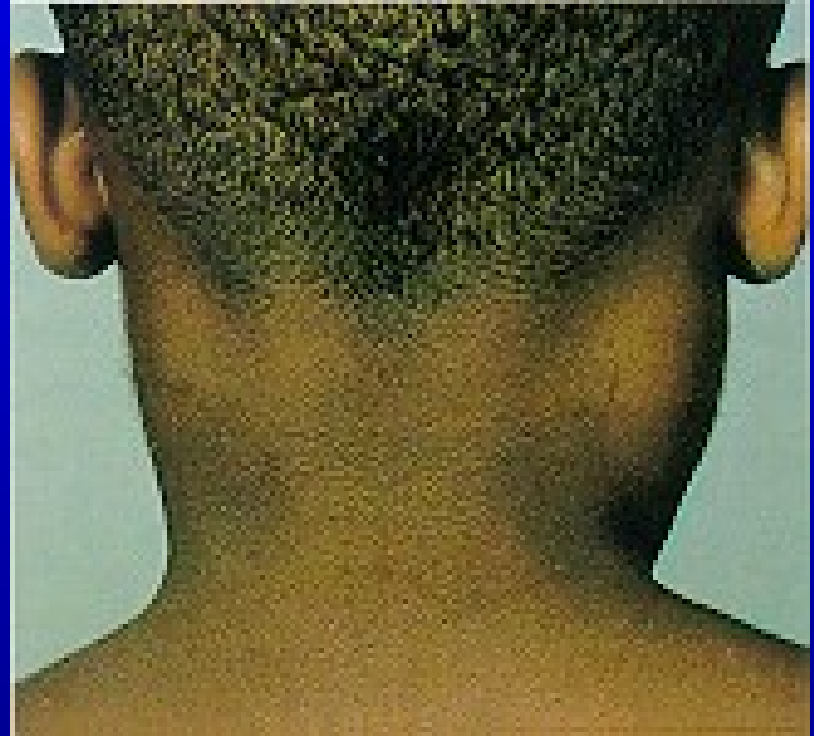
- URI viral or bacterial pharyngitis/tonsillitis - consider mono (EBV/CMV).
- head/neck tumors or thyroid ca



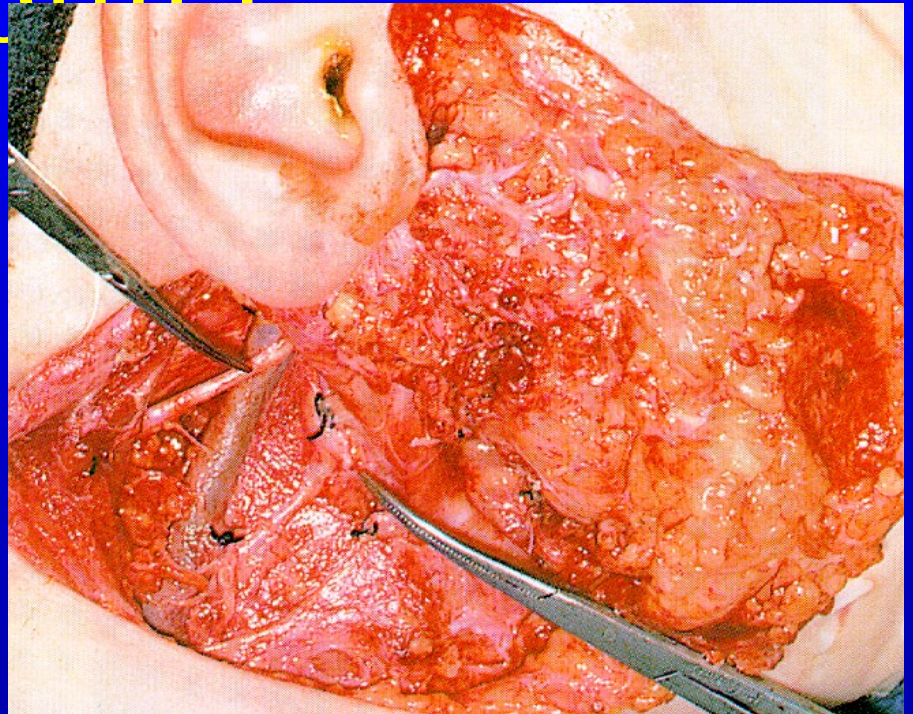


The Obligatory Netter-gram

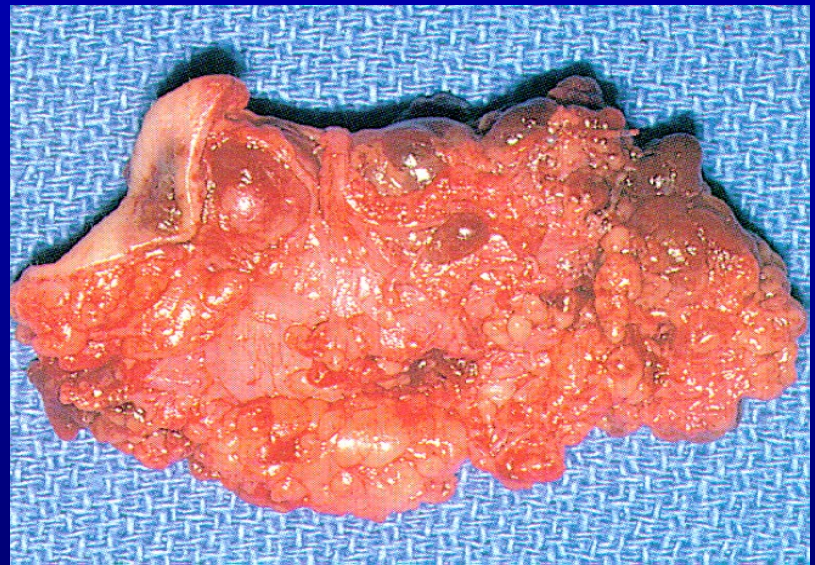
Posterior Cervical LAN - Mono



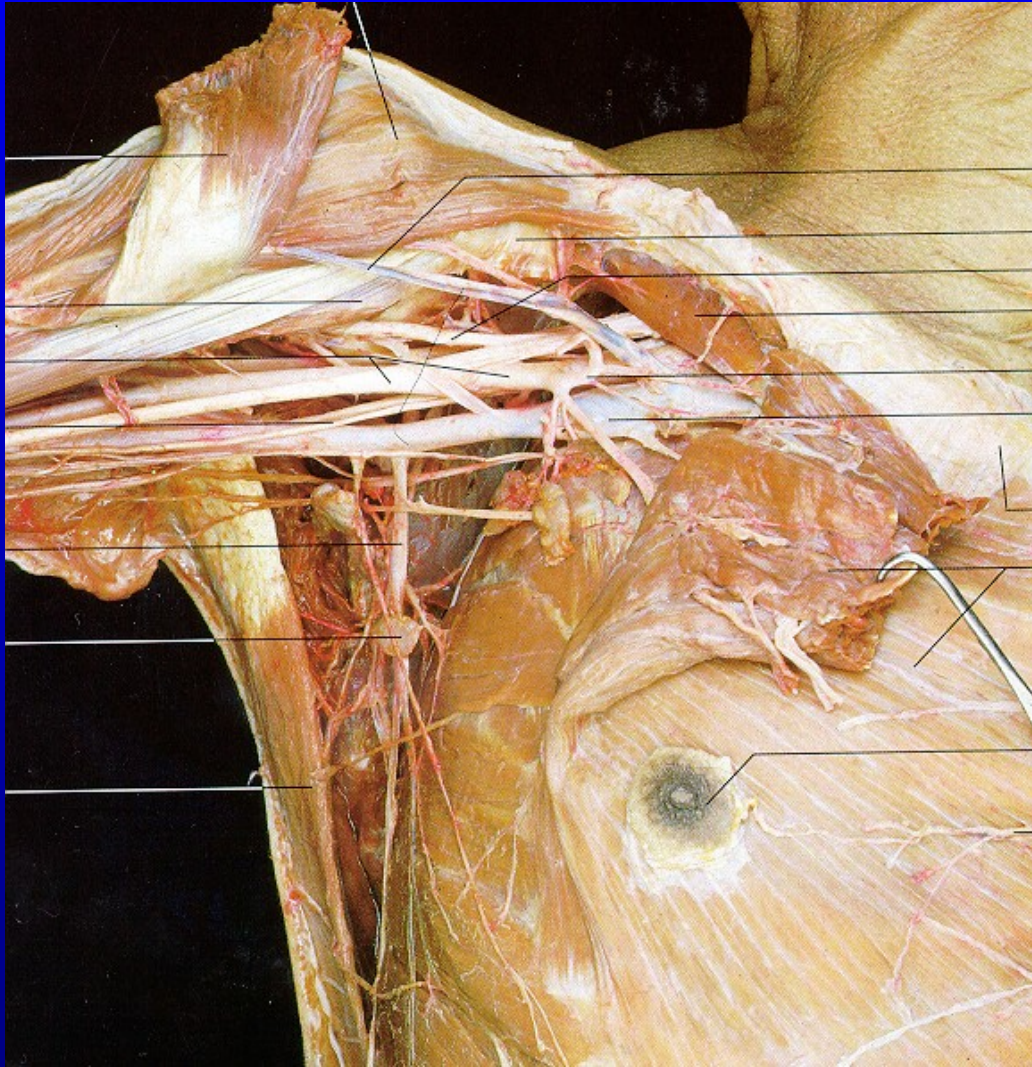
Mycobacterial Adenitis - “Scrofula”



Lymphatic spread of *M. tuberculosis* as well as atypical mycobacteria (*M. scrofulaceum*, MAI)



Axillary LAN



- nearby injury (hands/arms)
- cat-scratch dz
- breast cancer, melanoma
- silicone implants

Potentially fatal cat-scratch Dz



More common Cat- Scratch disease - *Bartonella Henselae*



Cat-Scratch Disease with characteristic axillary involvement



Unusual Clinical Presentation of Cat-Scratch - Perinaud's Oculoglandular Syndrome



Location of Nodes

- Supraclavicular - most commonly malignant
- If not malignant, then represents some other illness
 - MTB
 - Sarcoidosis
 - Histoplasmosis
 - Lymphoma (Hodgkin's and NHL)
 - Retroperitoneal Malignancy or Infection
 - Gastrointestinal Cancer (Virchow's Node)

Location of Nodes

- Mediastinal/Hilar
 - mono, MTB, sarcoidosis, histo/coccidioido, lymphomas, lung ca
- Intra-abdominal/retroperitoneal
 - Usually malignant (lymphoma vs germ cell vs pelvic neoplasm) though MTB can present with mesenteric lymphadenitis
- Periumbilical - Sister Mary-Joseph Node indicative of abdominal/pelvic neoplasm

Location of Nodes

- Inguinal
 - STD's (HSV, LGV, syphilis, gonorrhea, chancroid, granuloma inguinale)



Inguinal LAN



Inguinal LAN

- STD's
- Tinea infections (pedis/cruris)
- Pelvic/Genital Malignancy (squamous/melanoma)
- Bubonic Plague? - was there an exposure?
- Lymphoma

Directed Supportive Physical Exam Findings

General: Fever

HEENT: Pharyngeal erythema/exudate, peridontal dz. Petechiae, sinus tenderness, conjunctival infx/exudate

Abd: splenomegaly (assoc with EBV/CMV, sarcoid, lymphoma)

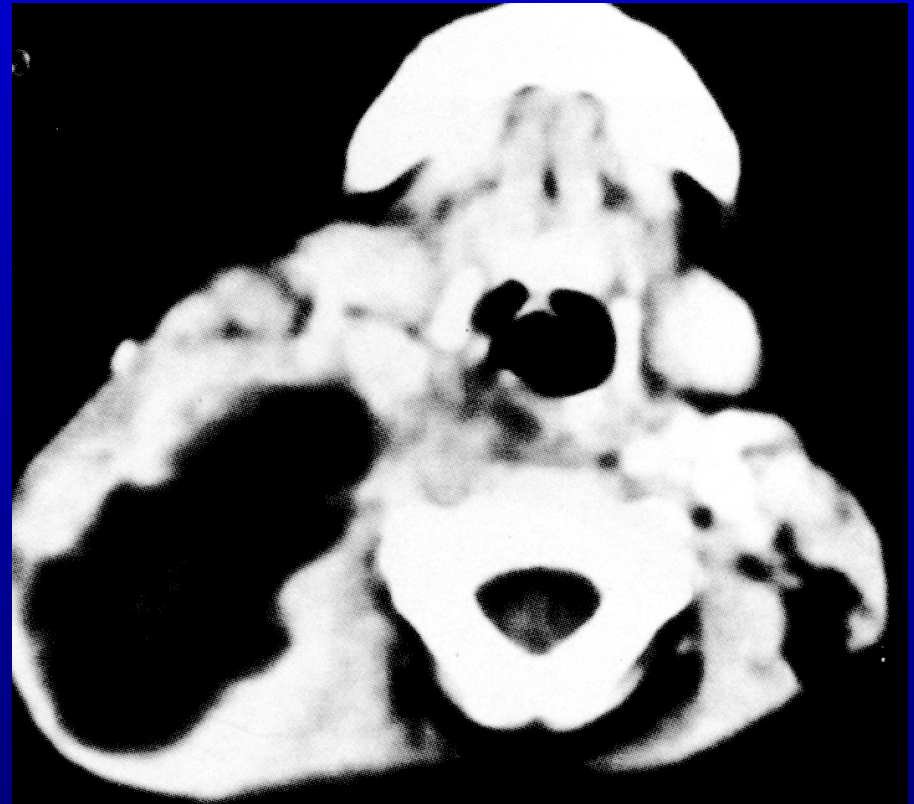
GU: discharge, ulceration, testicular mass, squamous ca

Ext: arthritis (SLE, Lyme's, Still's dz), proximal muscle weakness (assoc with dermatomyositis)

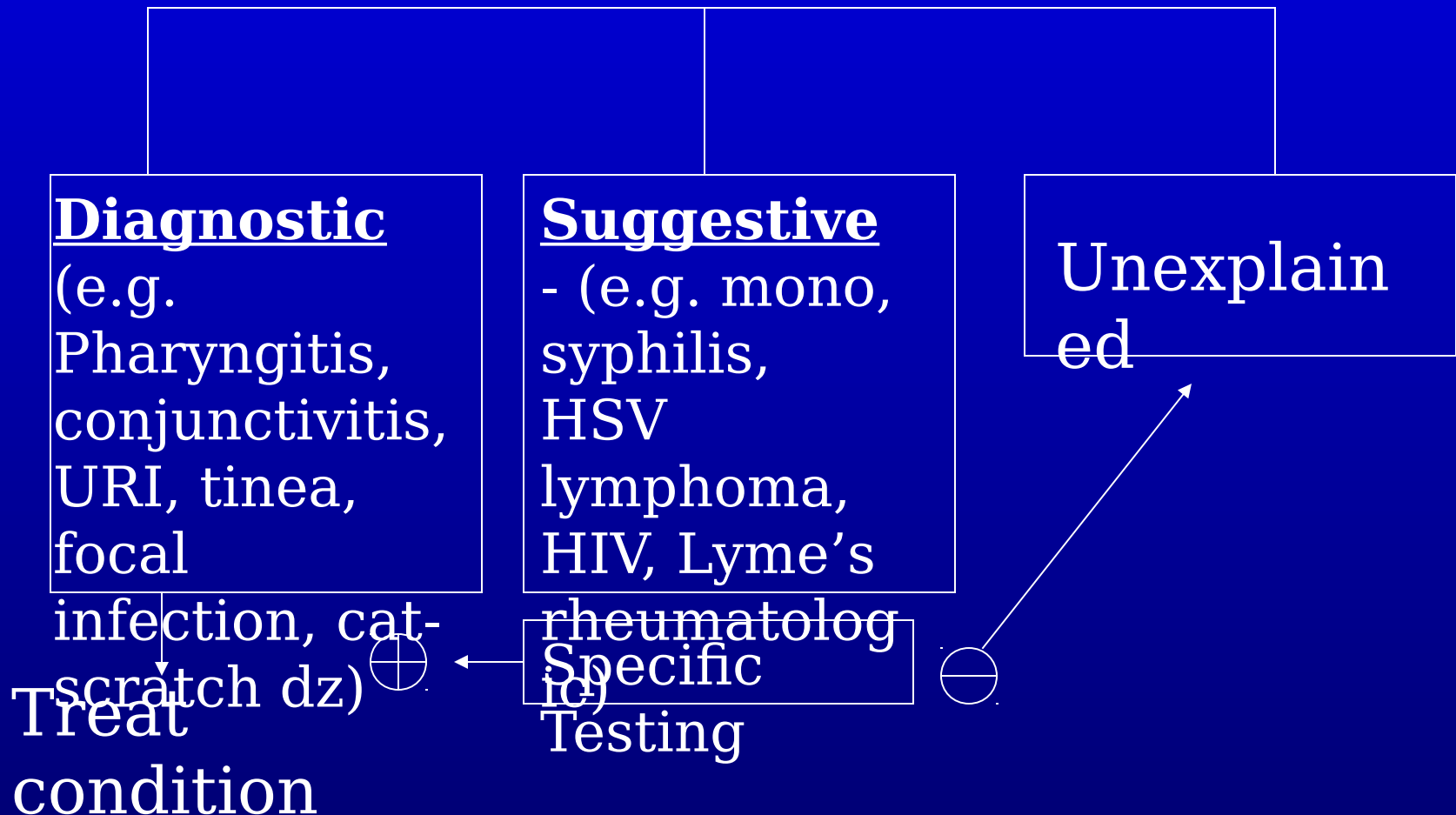
Skin: Rash (assoc with secondary syphilis, SLE, sarcoidosis, Kawasaki's, Lyme Dz, Measles, Rubella, Still's) Tinea infections (pedis/cruris) ulceration at

Be Aware of Complications

Suppuration/Abscess
Formation



Diagnostic Approach after History and Physical Examination



Supportive Labs for Suggested Causes

- Throat culture/Monospot
- EBV/CMV IgM, IgG,
- HIV
- CXR PA/Lat +/- PPD - if there is concern for granulomatous or lymphomatous disease
- CBC - eval for cytopenias, mono, infx
- Toxo IgM
- Lyme Titer
- RPR
- ANA, RF, CRP, C3+C4, CH50
- Hepatitis serologies

Eval of Unexplained LAN

- Is it localized or generalized?
- Generalized - indicates systemic disease is present
 - Review exposures/travel, review meds
 - If not helpful - CBC with manual diff and mono serologies
 - If not helpful - PPD, CXR, HIV, RPR, ANA, HepBsAg, Hep C Ab
 - If unrevealing, proceed to biopsy of most abnormal LN

Eval of Unexplained LAN

- Localized
 - Review History and exposure/travel clues
 - Examine regional area
 - If this is unrevealing, and LN > 1 cm, constitutional symptoms present, or signs of malignancy/serious illness, then proceed to Bx
 - If no risks for malignancy or serious illness (which includes most patients) observe for 3-4 weeks with scheduled follow-up visit.
 - If LN is same size or larger, proceed to biopsy

Examples of appropriate patient to refer on to biopsy

- Solitary hard cervical nodule in older patient with history of tobacco abuse
- Supraclavicular lymphadenopathy
- Generalized firm/rubbery lymphadenopathy with systemic symptoms

Rules for Excisional Biopsy

- Remember, by the time a patient is deemed appropriate for biopsy, the pre-test likelihood of malignancy increases to about 35% (29/82 in one series)
- Not unreasonable at this point to refer to Heme/Onc
- Use the largest/most abnormal node palpable.
- Avoid previously irradiated areas if possible
- Supraclavicular > cervical > axillary > > inguinal
- Coordinate ahead of time with surgeon and pathologist regarding appropriate specimen handling as some studies require fresh samples (and precluded by formalin preservation)

Biopsy Coordination

- Wright stains or H-E stains are available within minutes of biopsy and can be used to direct whether cultures or flow cytometry are needed
- Some tissue should be snap-frozen in all cases
 - For possible use in molecular genetics and future immunohistologic studies
- If site of biopsy difficult to reach (i.e. mediastinal/retroperitoneal), consider flow cytometry regardless of clinical picture

Guidelines for Eval of LN

Bx

Touch Prep	Small Lymphs	Mixed Small and Large Lymphs, no dysplastic large cells	Mixed Small and Large Lymphs and Occas Large Dysplastic Cell	Frequent Large Lymphocytes or Blasts
Freeze	Yes	Yes	Yes	Yes
Flow	Yes	Yes if clinically suggestive of NHL	Yes if clinically suggestive of NHL	Yes
Cytogenetics Molecular Genetics	Yes – to facilitate monitoring	No	No	Yes

No-No's of LAN

- Do not empirically prescribe antibiotics
 - Use them only if strong evidence for bacterial infx
- DO NOT use glucocorticoids unless LAN is life-threatening or sytemic illness dictates
 - eg. SLE flare, airway obstruction, cord compromise, SVC syndrome
 - Steroids can obscure some diagnoses (lymphomatous disorders)
 - Steroids and delay healing or activate indolent infections

Summary of LAN

- 1) Although LAN sometimes raises fears about serious illness, in patients seen in the primary care setting, it is usually the result of benign infections
- 2) MOST patients can be diagnosed on the basis of a careful history and physical exam
- 3) Local LAN should prompt a search for an adjacent precipitating lesion and examination of other nodal areas to r/o generalized LAN
- 4) Patients with nodes < 1.0 cm can be observed after excluding mono unless there are symptoms or signs of an underlying

Summary of LAN (cont)

- 5) LN > 1 cm are generally considered abnormal though inguinal LN can be up to 2 cm without concern for serious pathology
- 6) Supraclavicular LN are the most worrisome for malignancy and should proceed to biopsy early
- 7) Instructing the patient to return after 3-4 weeks observation is prudent with localized LAN and a benign picture
- 8) Generalized LAN should always prompt further clinical evaluation (Labs/CXR as appropriate)

